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IMPACT OF TOLERABILITY PROFILES ON HTA DECISION MAKING IN ONCOLOGY

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OBJECTIVES: To highlight the impact of tolerability profiles on Health Technology Assessment (HTA) decision making in non-small cell lung cancer (NSCLC), ovarian cancer and prostate cancer from three European HTA agencies. **METHODS:** HTA assessments on NSCLC, ovarian cancer and prostate cancer products marketed since 2011 were selected from HAS (France), G-BA (Germany) and NICE (UK). 14 reports on NSCLC, 5 on ovarian cancer and 14 on prostate cancer were selected for in-depth analysis. **RESULTS:** In the UK, safety profiles of the investigated drugs did not seem to have major impact on the recommendation. It was however seen that drugs with a good safety profile were more often recommended. Low impact of safety outcomes on the final decision from NICE was, for example, seen in the assessment of afatinib, where a significant increase in serious adverse events did not negatively impact the recommendation because clinical benefits outweighed safety concerns. Safety data and patient-relevance of endpoints is of high importance in Germany. A beneficial safety profile resulted in a higher benefit rating, whereas a negative safety profile lowered the G-BA rating. Case examples are evaluations of afatinib and crizotinib, where a negative safety profile lowered the benefit rating. Efficacy outcomes were weighted against safety outcomes in all assessments in France. An unfavourable safety profile appeared to have a negative impact on the ASMR rating from HAS, while a favorable profile did not have a positive impact. An example is the assessment of cabazitaxel, where the safety data presented at the initial submission was unfavorable, resulting in a lower ASMR rating (IV), however a resubmission with additional safety data resulted in a higher rating (III). **CONCLUSIONS:** Different EU payers seem to have a different view on safety profiles, with the highest impact seen in Germany and the lowest impact seen in the UK.

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HIERARCHY OF CLINICAL ENDPOINTS IN HTA DECISION MAKING IN ONCOLOGY

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OBJECTIVES: To highlight the hierarchy of clinical endpoints in Health Technology Assessment (HTA) decision making in NSCLC, ovarian cancer and prostate cancer from three European HTA agencies. **METHODS:** HTA assessments on non-small cell lung cancer (NSCLC), ovarian cancer and prostate cancer products marketed since 2011 were selected from HAS (France), G-BA (Germany) and NICE (UK). 14 reports on NSCLC, 5 on ovarian cancer and 14 on prostate cancer were selected for in-depth analysis. In addition ASCO and ESMO guidelines were reviewed for recommendations around endpoints. **RESULTS:** HTA agencies base their decisions on the significance of the presented outcomes, but an analysis of NSCLC assessments showed that when the effect sizes in overall survival (OS) and progression-free survival (PFS) were deemed to be clinically irrelevant, recommendations were less positive. Significant improvements in OS and PFS can still be rejected in the UK because of unacceptable cost-effectiveness. Assessments demonstrating improvements only in PFS were most of the time rejected. Significant improvements in OS were associated with a higher ASMR rating in France. Assessments with improvements in surrogate outcomes, including PFS and overall response rate, were also accepted. OS and quality of life (QoL) are the main outcomes contributing to the benefit rating in Germany. A combination of OS and QoL improvements was associated with a higher G-BA benefit rating. When OS or QoL data were absent, the benefit rating was lower. **CONCLUSIONS:** OS data is considered the gold standard for clinical benefit in oncology, but surrogate outcomes and QoL benefits were also accepted when non-significant OS results were seen. In addition, it seems that statistical significance in itself is not enough, as payers want to see a clinical meaningful difference. Further research in pancreatic, breast and colon cancer, for which thresholds for clinical relevance have been published recently, could validate these results.

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IS THERE AN IMPACT OF THE ORPHAN DESIGNATION IN ONCOLOGY ON MARKET ACCESS IN EUROPE?

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OBJECTIVES: Orphan drugs (ODs) benefit from incentives from EMA for their development, but in a context of economical restrictions payers are more and more worried by highly priced medicines. The aim of this research was to evaluate whether the orphan designation has an impact on the reimbursement and pricing for drugs in oncology in European coutries. **METHODS:** First, a literature review was performed to identify specific methodologies or consideration applied for the evaluations of ODs. Second, a comparative analysis of HTA recommendations for drugs registered for their first indication in oncology between 2006 and 2013 and appraised by four agencies (HAS, G-BA, NICE, SMC) was performed, as well as coverage decisions, treatment cost, and delay between approval and price agreement. **RESULTS:** In the selected countries, there is no specific methods to assess ODs. However some special considerations are made to accept higher level of uncertainty. 49 drugs were included in the analysis. Significant inter-country variability in the HTA recommendations exists: 20% of drugs received heterogeneous recommendations across countries. The highest concordance scores were obtained between NICE and SMC for ODs (0.9 kappa score), for others concordance was poor. The percentage of rejection for ODs was not higher than the one for non-ODs. Average treatment costs were in favour of orphan oncology drugs, still it was not significant. There was correlation between treatment cost and population size for the non-ODs, but it was not the case for ODs. Delay of appraisal for ODs was slightly shorter, but never significant, except for NICE. **CONCLUSIONS:** In this study we did not show a significant advantage or disadvantage in the market access of ODs in oncology. However, as more ODs will obtain regulatory approval on an accelerated or conditional licensing, providing expanded evidence package to show the value for money to payer will become harder.

PCN181

OPTIMISING MARKET ACCESS OF CANCER DRUGS IN CANADA: A STUDY OF ECONOMIC REVIEWS BY THE PAN-CANADIAN ONCOLOGY DRUG REVIEW (PCODR) EXPERT COMMITTEE

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OBJECTIVES: pCODR was established in 2010 to guide drug funding decisions through assessing the clinical, patient perspectives and cost-effectiveness (CE) information of new drugs. A considerable number of oncology drugs do not get recommended or get conditional recommendation. This study aims to analyse the comments provided in pCODR final recommendations and act as a guidance for manufacturers to improve the preparation of pCODR submissions. **METHODS:** A review of pCODR assessments was completed evaluating all recommendations made available between May 2012 and December 2014 (N=36) relating to 29 oncology drugs. The comments regarding CE estimates were extracted and analysed based on the assessments made available on the website. **RESULTS:** In the reviewed recommendations, 3 drugs received a positive unconditional recommendation (8%), 26 received a positive recommendation, conditional on the cost-effectiveness being improved to an acceptable level (72%) and 7 were not recommended for funding (20%). Comments on CE estimates were analysed and summarised, the most prevalent comments received included lengthy time horizon (n=13), uncertainty (clinical benefits, large variability in the estimates, ICER sensitive to changes in overall survival) (n=11), lack of clinical evidence (n=9), inadequate model structure (n=5), invalid clinical assumptions (n=5) and the effects of potential wastage on ICER (n=3). **CONCLUSIONS:** This review suggests that in order to minimise comments that might hinder a favourable recommendation, manufacturers need to focus on demonstrating the CE of a drug over a time period in which parameters are more certain (e.g. trial horizon), as well as trying to generate clinical evidence to prove benefits of a drug beyond trial period. The investigators are currently evaluating other aspects of the review deliberative framework (clinical benefit, patient-based values and adoption feasibility) with the aim to develop a more comprehensive guideline for manufacturer's future submissions.

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USE OF MOLECULAR TESTING PRIOR TO FIRST-LINE ERLOTINIB THERAPY AMONG MEDICARE PATIENTS WITH STAGE IV NON-SMALL CELL LUNG CANCER

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OBJECTIVES: The extent to which individual lung cancer patients undergo guideline-recommended molecular testing in routine care prior to initiation of first-line erlotinib is not known. Prevalence and factors associated with testing and erlotinib therapy were determined in Stage IV non-small cell lung cancer (NSCLC). **METHODS:** We identified incident cases diagnosed between 2007-2009 using SEER-Medicare data. Multivariable models were used to identify factors independently associated with (1) molecular testing and (2) receipt of first-line erlotinib therapy. **RESULTS:** Only 6.5% (500/7,678) were treated with first-line erlotinib and of those, only 8.6% underwent a molecular test. Testing and erlotinib therapy were independently associated with phenotypic enrichment using correlates of epidermal growth factor receptor (EGFR) mutations (female gender, Asian ethnicity, non-squamous-cell histology). Older age, Medicaid enrollment, and admission to hospice decreased likelihood of testing but increased probability of erlotinib therapy. **CONCLUSIONS:** Vast majority of NSCLC patients did not undergo molecular testing prior to treatment. Clinical enrichment criteria were influential in patient selection for erlotinib therapy and testing, but these attributes do not adequately discriminate between EGFR mutation positive and wild type tumors. Provider education and payer mandates to submit test results before reimbursement for targeted therapies may encourage guideline-recommended implementation of these technologies.

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ONCOLOGY DRUGS RECEIVING BREAKTHROUGH THERAPY DESIGNATION: CLINICAL TRIAL CHARACTERISTICS, DRUG PRICING, AND APPROVAL PROCESS

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OBJECTIVES: The Food and Drug Administration (FDA) grants breakthrough therapy designation (BTD) to facilitate faster approval of drug products are intended to treat a serious or life-threatening condition or provide substantial improvement over existing therapies. The purpose of this review is to compare time to approval, treatment cost and key clinical design characteristics of BTD drugs to non-BTD drugs in oncology. **METHODS:** This narrative review used publicly reported data from drug manufacturers' and FDA websites to examine all oncology drugs approved between November 2013 and December 2014. Median time-to-approval was assessed for new molecular entities (NMEs) and monthly treatment cost was calculated for approved indications based on wholesale acquisition cost (WAC) from Analysource. Approved oncology drugs were categorized as BTD and non-BTD drugs for comparison. **RESULTS:** A total of 25 FDA indications for oncology drugs were approved from November 2013 to December 2014. Nine indications were granted BTD, while 16 were approved through non-BTD pathways. For NMEs, median time from phase 1 trial initiation to indication approval was 2 times longer for non-BTD drugs (3414 days) compared to BTD drugs (1732 days). Pivotal trials had a median sample size of 173 participants and 213 participants for BTD and non-BTD drugs, respectively. For BTD drugs, pivotal trials were 44% phase 2, 44% single-arm, and 89% open-label studies. For non-BTD drugs, pivotal trials were 44% phase 2, 28% single-arm, and 69% open-label studies. Median treatment cost was $9,249 per month for BTD drugs and $10,099 per month for non-BTD drugs. **CONCLUSIONS:** The BTD approval pathway has offered a considerably shorter time-to-approval for oncology drugs. Trials leading to approval for BTD drugs had a higher proportion of single-arm and open-label studies compared to non-BTD drugs. Our findings suggest that oncology drugs with BTD are not related to higher treatment cost.